Remarks

Upon entry of this amendment, claims 183-200 will be pending in the above-captioned application. Claims 183, 189, and 195 have been amended to recite "wherein said polypeptide binds to an antibody that specifically binds a polypeptide consisting of the amino acid residues of SEQ ID NO:2." Support for this amendment is found in the specification as filed, for example, at page 39, lines 5-10; at page 41, lines 8-11; and at page 66, line 18 to page 67, line 1.

Accordingly, no new matter has been introduced and entry of this amendment is respectfully solicited.

I. Information Disclosure Statement

The Examiner has indicated that the IDS which was filed on 25 September 2002 as Paper No. 19 is duplicative of the IDS which was filed on 04 May 2000 as Paper No. 4. *See*, Paper No. 22, page 3, paragraph 6.

Applicants respectfully disagree. The references listed in Paper No. 19 are different than the references listed in Paper No. 4. However, Applicants note that two of the references are related. The first, reference AN6, listed in Paper No. 19, is a new search report published in relation to reference AO2, International Publication No. WO 95/24928, listed in Paper No. 4. The second, reference AR24, listed in Paper No. 19, was previously brought to the Examiner's attention in the Information Disclosure Statement filed on 04 May 2000 as a part of Paper No. 4 and a copy of which is now being provided and cited in Form SB/08 of Paper No. 19. Accordingly, Applicants respectfully request the Examiner to consider the references cited in Paper No. 19.

II. Double Patenting Rejection

The Examiner has alleged that the instant application may have conflicting subject matter with U.S. Application No. 10/075,446 and U.S. Patent Nos. 6,077,692 and 6,238,888. In particularly, the Examiner asserts that language of binding an antibody that specifically binds amino acids Ser (69) - Ser (208) of SEQ ID NO:2 in conjunction with the percent identity language of the claims constitutes new matter and if canceled from the claims would render a double patenting rejection appropriate. *See*, Paper No. 22, Page 3, paragraph 7.

Applicants have not canceled this language, but rather have amended claims 183, 189, and 195 to recite "wherein said polypeptide binds to an antibody that specifically binds a polypeptide consisting of the amino acid residues of SEQ ID NO:2." For the reasons developed below, Applicants believe that the claims, both as amended and as rejected, are fully contemplated and described in the instant specification. Thus, Applicants assert that the subject matter of the instant application and the subject matters of U.S. Application No. 10/075,446 and U.S. Patent Nos. 6,077,692 and 6,238,888 do not conflict and a double patenting rejection is improper.

III. Written Description Rejections

a. The Examiner has rejected claims 183-200 under 35 U.S.C. § 112, first paragraph as allegedly containing new matter. In particular, the Examiner alleges that

> ...[t]here is no disclosure of percent sequence identity in conjunction with the polypeptide comprising amino acids 69-208 of SEQ ID NO:2. Secondly, there is no disclosure of percent sequence identity in conjunction with a polypeptide that binds an antibody that specifically binds the polypeptide of SEQ ID NO:2.

See, Paper No. 22, page 4, paragraph 9.

Applicants respectfully disagree and traverse this rejection. Applicants have amended claims 183, 189, and 195 to recite "wherein said polypeptide binds to an antibody that specifically binds a polypeptide consisting of the amino acid residues of SEQ ID NO:2." For the reasons developed below, Applicants believe that the claims, both as amended and as rejected, are fully described in the instant application.

Applicants assert that the instant specification clearly contemplates polypeptides with percent identity in conjunction with deletion mutants, specifically amino acids Ser (69) - Ser (208) of SEQ ID NO:2. For example, the specification states at page 36, lines 10-16 that

> [t]he polypeptides of present invention include the polypeptide of SEQ ID NO:2 (in particular the mature polypeptide) as well as polypeptides which have at least 90%, 95%, 96%, 97%, 98%, 99% similarity (more preferably at least 90%, 95%, 96%, 97%, 98%, 99% identity) to the polypeptide of SEQ ID NO:2 *and also include portions of such polypeptides* with such portion of the polypeptide (*such as the deletion mutants* described below) generally

> containing at least 30 amino acids and more preferably at least 50 amino acids.

(Emphasis added). Deletion mutants are further described as including amino acids "Ser (69) -- Ser (208)." *See*, specification, for example, at page 45, line 29; at page 46, lines 1-3; and at Example 16, at page 136, line 15 to page 139, line 10. Thus, the specification clearly links percent identity to deletion mutants, including Ser (69) - Ser (208) of SEQ ID NO:2.

The specification also links deletion mutants that can be bound by an antibody that specifically binds SEQ ID NO:2. For example, the specification states on page 66, line 29 to page 67, line 1 that "[i]n this manner, even a sequence encoding only a fragment of the polypeptides can be used to generate antibodies binding the whole native polypeptides." Additionally, the specification describes how "polypeptides of the invention" (which include deletion mutants with percent identity) are "therefore useful to raise antibodies, including monoclonal antibodies, that bind specifically to the polypeptide of the invention." *See*, for example, page 39, lines 5-7; *See also*, page 66, lines 2-29. Thus, the specification clearly teaches polypeptides of the invention, which include deletion mutants of a specified percent identity, in conjunction with binding an antibody that specifically binds SEQ ID NO:2.

In summary, Applicants contend that the claims of the instant application are fully described by the specification as filed. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of the instant claims under 35 U.S.C. § 112, first paragraph for new matter.

b. The Examiner has further rejected claims 183-200 under 35 U.S.C. § 112, first paragraph for alleged lack of written description. In particular, the Examiner contends that

> ...[t]he specification does not provide a complete structure of those molecules which have the recited % sequence identity to SEQ ID NO:2 and retain the required function of the claims. The claims also fail to recite other relevant identifying characteristics ... sufficient to describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus because the specification teaches a single embodiment.

See, Paper No. 22, paragraph spanning pages 6-7.

Applicants respectfully disagree and traverse. Applicants have amended claims 183, 189, and 195 to recite "wherein said polypeptide binds to an antibody that specifically binds a polypeptide consisting of the amino acid residues of SEQ ID NO:2." For the reasons developed below, Applicants believe that the claims, both as amended and as rejected, are fully described in the instant application.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. (*See*, M.P.E.P. § 2163(I) at 2100-15, and *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991)).

The Federal Circuit has re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed,'" *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.PQ.2d 1227 (Fed. Cir. 2000). Further, the Federal Circuit has emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification; and not whether the specific embodiments had been explicitly described or exemplified. Indeed, the court noted that "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d at 1001, (emphasis added).

Thus, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability based on lack of written description by presenting evidence or reasons why one skilled in the art would *not* reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, the Examiner has not met this burden.

Moreover, Applicants submit that the Examiner cannot meet the burden of presenting a *prima facie* case of unpatentability, because the specification describes with reasonable clarity to one of skill in the art that the inventors were in possession of the claimed invention on the earliest filing date of the present application. Applicants further

submit that the Examiner has underestimated both the teaching of the present application and the level of skill in the art on the priority date of the present application.

Applicants submit that the Examiner is in part relying on language regarding a "representative number" of a claimed genus set forth in *Regents of the University of California v. Eli Lilly & Co.*, (119 F.3d 1559, 1569, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997)) and incorporated into the Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement ("Guidelines"), when reciting the procedures followed in analyzing whether the description requirement for each of the claims at issue is satisfied. However, even assuming, *arguendo*, that the Guidelines comport with the law, the Guidelines also define a "representative number" as "an inverse function of the skill and knowledge of the art." *See* Guidelines at Page 1106. Applicants note that the level of skill in the art on the priority date of the present application was very high.

Furthermore, the central issue in *Eli Lilly* involved claims to mammalian cDNAs encoding insulin, which were supported in the specification only by the nucleotide sequence for the rat insulin gene. The Federal Circuit found the claims lacking in written description because the claims defined only a result or function. The court held that a result or function will satisfy the written description requirement *only if* correlated to a description of structural features of the claimed invention. According to the court, a sufficient written description must allow the skilled artisan to "visualize or recognize the identity of the members of the genus." *Id.*

Applicants contend that the instant specification provides a sufficient written description as mandated in *Eli Lilly*. In particular, Applicants submit that the specification provides ample written description to enable one of skill in the art to visualize or recognize the identity of the members of the claimed genus. For example, the specification provides the skilled artisan with the detailed structure of the polypeptides of the invention, *e.g.*, the amino acid sequence of the N-terminal deletion mutant Ser (69) - Ser (208) of SEQ ID NO:2, herein referred to as KGF-2Δ33. *See*, for example, specification at page 46, lines 1-3 and at page 139, lines 6-10.

In addition to the amino acid sequence common to the polypeptides of the claimed invention (e.g., KGF-2Δ33), the specification further provides ample disclosure of other relevant characteristics of the claimed polypeptides. First, the specification provides the

parameters used to determine the percent identity of the polypeptides of the claimed invention. *See*, for example, specification at page 36, line 10 to page 37, line 25. The specification further provides a detailed analysis of the structural attributes of the KGF-2 protein, including preferred amino acid substitutions and point mutations, many of which are encompassed within the scope of the claims. *See*, for example, specification at page 11, line 22 to page 12, line 3, at page 29, line 28 to page page 30, line 30, at page 35, lines 3-19; page 50, line 26 to page 53, line 3; at Example 22, page 152, line 1 to page 160, line 10; and at Figure 4A-4E. Moreover, the specification provides specific N-terminal and C-terminal deletion mutants of SEQ ID NO:2, for example, Ala (63) - Ser (208), Val (77) - Ser (208), and the six examples of point mutants of KGF-2Δ33 disclosed in Example 22, all of which fall within the scope of the instant invention. *See*, specification, for example, at page 16, lines 1-6; at page 44, line 27 to page 50, line 2, at Example 22, page 152, line 1 to page 160, line 10; and at Figures 26 and 27.

The specification also provides a detailed analysis of the functional attributes of the KGF-2 protein, such as, for example, antigenic index of the KGF-2 polypeptide. *See*, specification, for example, at page 11, line 22 to page 12, line 3, and at Figure 4A-4E. In particular, the specification discloses specific antigenic and hydrophilic regions of the KGF-2 protein. *See*, specification, for example, at page 40, lines 7-16; page 53, line 20 to page 54, line 9; and at Figure 4A-4E. Many of these antigenic and hydrophilic regions completely fall within the amino acid sequence of KGF-2Δ33. The specification further teaches the use of the polypeptides of the invention, including the polypeptides with percent identity to KGF-2Δ33, for generating antibodies that specifically bind a polypeptide of SEQ ID NO:2. *See*, specification, for example, at page 39, lines 5-10; at page 41, lines 8-11; and at page 66, line 18 to page 67, line 1.

Accordingly, one skilled in the art, enlightened by teachings of the present application, could readily envision countless polypeptide sequences that comprise the specified polypeptides. For example, the skilled artisan could clearly envision each of the polypeptides that are 90% identical to KGF-2Δ33 as a polypeptide with at least 1, 2, 3, 4, etc. amino acid substitutions or deletions along its length. Indeed, nothing more than a basic knowledge of the genetic code and what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides that are

90% identical to KGF-2Δ33. Clearly, such knowledge is well within what is expected of the skilled artisan.

Thus, the instant claims clearly distinguish the boundaries of each claimed genus and identify all of the members of each genus. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims, upon reading the present application as filed.

Accordingly, from reading the specification, the skilled person would immediately recognize that, at the time the specification was filed, the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563); namely, a genus of proteins comprising polypeptides with 90%, 95%, or 97% identity to the amino acids of Ser (69) - Ser (208) of SEQ ID NO:2, wherein said polypeptides bind an antibody that specifically bind a polypeptide consisting of the amino acid residues of SEQ ID NO:2. Therefore, the specification contains an adequate written description of the claimed polypeptides.

For all of the above reasons, Applicants respectfully assert that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claim 183-200 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the above-made remarks and amendments be entered and made of record in the file history of the instant application. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the allowance of this application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

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Respectfully submitted,

By _____

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